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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 10/522,986 | 09/13/2006 | Piero Del Soldato | 026220-00061 | 6969 |
| 4372 | 7590 | 05/02/2008 | | |
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| EXAMINER | | | | |
| LAO, MARIA LOUISA | | | | |
| ART UNIT | | PAPER NUMBER | | |
| 1621 | | | | |
| NOTIFICATION DATE | | DELIVERY MODE | | |
| 05/02/2008 | | ELECTRONIC | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DCIPDocket@arentfox.com
IPMatters@arentfox.com
Patent_Mail@arentfox.com

Office Action Summary

Application No.

10/522,986

Applicant(s)

DEL SOLDATO ET AL.

Examiner

LOUISA LAO

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 February 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 2 and 11-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-10, 24-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-8508)
- Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Response to Arguments

1. Applicant's arguments filed 2/12/08 have been fully considered, with respect to the:
 - a. objections of claims (3 and 4) and (4 and 6-10) in light of the amendments are persuasive. The objections have been withdrawn.
 - b. new claims 24-26 are acknowledged;
 - c. rejection of claims 1 and 3 under 35 U.S.C. 103(a) but they are not persuasive, see below. The rejection is maintained.
2. The election of species, (E)-3-(4-hydroxy-3-methoxyphenyl)-2-propenoic acid 4-nitrooxybutyl ester is still applicable in the examination of the claims.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

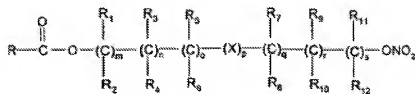
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

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made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. The rejection of claims 1 and 3 is maintained under 35 U.S.C. 103(a) as being unpatentable over Del Soldato (US5861426, US'426).
5. The instant claims are drawn to a process for preparing a compound of the general

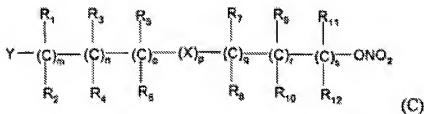


(A)

formula , with the

substituents defined therein. The process comprising the reaction of a compound of formula (B)

R-COO-Z, with a compound of formula (C), as shown



(C)

, and the substituents as

recited therein.

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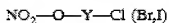
6. US'426 teaches nitro compounds of the formula $A-X_1-NO_2$ (see Abstract).

New compounds and their compositions having anti-inflammatory, analgesic and anti-thrombotic activities, of the general formula: $A-X_1-NO_2$ or their salts, wherein: A is $R(COX_u)_t$, wherein t is zero or 1 and u is zero or 1; and X is O, NH or NR_{1C} wherein R_{1C} is C_1-C_{10} alkyl; and R is (Ia) wherein R_1 is acetoxoy, preferably in ortho-position with respect to $-CO-$ and R_2 is hydrogen; or derivatives of acetylsalicylic acid; and X_1 is $-YO-$ wherein Y is C_1-C_{20} alkylene, C_5-C_7 cycloalkylene, oxy-alkyl derivatives and oxy-methyl benzyl derivatives.

In columns 15- 16, US'426 teaches the synthetic route by which these compounds are achieved.

In particular, US'426 teaches in column 16 lines 3-14

An alternative route to form the esters is a reaction of the sodium or potassium salts of the acids with the nitric esters of halogen alcohols of the general formula:



to directly give the products of the invention.

) The reaction route is as follows:

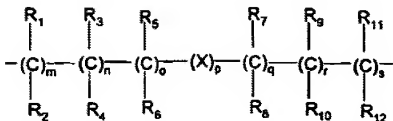


wherein YO is X_1 .

The synthetic scheme outlined by US'426 is generically embraces the instant process, as well as teaching structurally similar compounds. The structurally similar compounds are correspondingly where $R-CO-O-Na$ is instant compound of formula [B] and $Br-Y-NO_2$ is instant compound of formula [C] and $R-CO-O-Y-NO_2$ is compound of formula [A].

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7. The difference from the claimed process and the prior art is that the prior art is directed to a broader genus. US'246 differs from the instant claims in the substituents of the instant compounds of formula [B] , formula [C] and formula [D] ; illustratively, when X_1 of US'246 corresponds to formula [C] is



8. This difference would not have been patentable because it would have been obvious, at the time of that Applicants' invention was made, to one of ordinary skill in the art to have employed a method to prepare nitrooxyester compounds or derivatives thereof with the teachings of US'246; with a reasonable expectation that the sub-genus would have a utility of the genus as a whole.

9. An artisan would have been motivated to employ the process scheme delineated by US'246 since the steps thereto show the generic reaction of a carboxylic salt and a nitroxyhalide to form a product that embraces a generic version of instant formula [A] and the artisan would reach a reasonable expectation of success of preparing nitrooxyesters of the instant claims.

10. The instant claims are rendered obvious by the cited prior art reference.

- Applicants amended claim 1 by deleting $Y = Cl, Br$ and I . Applicants allege that the teachings of the cited prior art reference was because of hindsight and that one of ordinary skill in the art would have no motivation to utilize the teachings of US'246 to arrive at the instant process.

However, Applicants' allegations are flawed because US'246 embraces the instant process and shows the mechanics thereto. It would not be inconceivable by one of ordinary skill in the art to start with the teachings of US'246; since US'246 teaches the process of making nitro-oxyl derivatives; and shows alternate schematic routes thereto.

- The claims would have been obvious because "a person of ordinary skill has good reason to pursue the known options within his grasp, such as the adaptation of techniques that have been proven to work in his field of endeavor. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense."
- The Supreme Court in *KSR* noted that if the actual application of the technique would have been beyond the skill of one of ordinary skill in the art, then the resulting invention would not have been obvious because one of ordinary skill could not have expected to achieve it.

Thus, Applicants' arguments are unpersuasive.

11. Claims 1, 3-10 and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Del Soldato (US5861426, US'426 equivalent to WO95/30641 *in ISR*) or Del Soldato et al. (US7199258, US'258).

12. US'426, as discussed *supra*, is included herein in its entirety.

(Note: Applicants amended claim 1 to limit the definition of X; but claim 4 still carries the amended limitation of X).

13. US'258 teaches a process for preparing nitrooxyderivatives of naproxen, of general formula (A), comprising reacting a compound of formula (B) with compound of formula (C) (col2-5). US'258 teaches these reactions in examples (Examples 1-4). See also claims 1-8, where US'258 teaches the reaction conditions, solvents and molar ratios,

14. The difference between the instant claims and US'246 has been discussed *supra*. See ¶6-10 and the ensuing "Response to Applicants' Arguments" are included herein, in their entirety.

15. The instant claims differ from US'258 in the substituent R of formula (A).

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16. The difference, however, would not be patentable because it would have been obvious to one of ordinary skill in the art to use alternate or equivalent materials to arrive at other nitrooxyderivatives of general formula (A),

17. The artisan would have been motivated to start with the teachings of US'258 since US'258 has shown that the reaction of compounds of formula (B) with formula (C) lead successfully to compounds of formula (A); and the artisan would reach a reasonable expectation that in utilizing equivalent alkoxyaryl-compounds for R that he can make other nitrooxyderivatives of general formula (A) or naproxen.

18. No claims are allowed.

Conclusion

19. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. References in ISR of WO2004020384 and WO2004020385; Del Soldato (US5700947 equivalent to WO95/09831 *in IDS*); Del Soldato (US5780495); including the NPL documents therein.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louisa Lao whose telephone number is (571)272-9930. The examiner can normally be reached on Mondays to Thursdays from 8:00am to 8:00pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

0420-252008ml

/Karl J. Puttlitz/

Primary Examiner, Art Unit 1621

Louisa Lao

Examiner

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